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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/701,278	08/22/96	ANDERSON D	A-63770-1/RF

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EXAMINER	
HAYES,R	

ART UNIT	PAPER NUMBER
1817	

DATE MAILED: 11/25/97

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
08/701278	Anderson et al.
Examiner	**Group Art Unit**
Hayes	1817

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Response

A SHORTENED STATUTORY PERIOD FOR RESPONSE IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a response be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for response specified above is less than thirty (30) days, a response within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for response is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication .
- Failure to respond within the set or extended period for response will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

☒ Responsive to communication(s) filed on 8/18/97.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle,* 1935 C.D. 1 1; 453 O.G. 213.

Disp sition of Claims

☒ Claim(s) 1-19 is/are pending in the application.

Of the above claim(s) 8-17 is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1-7, 18-19 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☒ Claim(s) 1-19 were ~~are~~ subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Pri rity under 35 U.S.C. § 119 (a)-(d)

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 11 9(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received: _____.

Attachment(s)

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 9

☐ Interview Summary, PTO-413

☒ Notice of References Cited, PTO-892

☐ Notice of Informal Patent Application, PTO-152

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Other _____

Office Acti n Summary

DETAILED ACTION

Election/Restriction

1. Applicant's election without traverse of Group I, claims 1-7, in Paper No. 8 is acknowledged. Claims 8-17 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b) as being drawn to a non-elected . Election was made **without** traverse in Paper No. 8.

Claim Objections

2. The numbering of claims is not accordance with 37 CFR 1.126. The original numbering of the claims must be preserved throughout the prosecution. When claims are canceled, the remaining claims must not be renumbered. When claims are added, except when presented in accordance with 37 CFR 1.121(b), they must be renumbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not).

Misnumbered new claims 15-16 have been renumbered 18-19.

Claim Rejections - 35 U.S.C. § 112

3. Claims 1-3, 5-7 & 18-19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the nucleic acid depicted as SEQ ID NO 1, does not reasonably provide enablement for any hybridizable fragment of these polynucleotides, or vectors,

host cells, or methods whose sole purpose is to produce an uncharacterized DRG11 protein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification states on page 2 that "it is an object of the present invention to provide a marker to identify neurons in the peripheral sensory lineage". Page 29 discloses that "DRG11 is closely related *in sequence* to PAX3 as well as to several other paired homeodomain proteins" [emphasis added]. Page 33 then discloses that "[w]hether the apparent lack of DRG11 expression in other sensory neurons reflects distinct sensory lineages, or rather environmental modulation in culture, is *currently being investigated*". Finally, page 34 states that DRG11 is a "*putative* transcription factor" which is "*likely* to regulate later-developing aspects of sensory neuron phenotype or function"; and may possibly be "important in appropriate synapse formation" [emphasis added]. However, no assays to determine what function the DRG11 protein actually possesses are disclosed, or known; nor are any diseases states disclosed that are specifically correlated with DRG11 gene dysfunction. In fact, there is no disclosure in the specification on defining *any* function that is actually known to be inherent to the isolated DRG11 protein of the instant invention. Moreover, the instant specification describes only rat DRG11 nucleic acid molecules; thereby, providing a deficient written description of what structurally constitutes the DRG11 family, as encompassed by the current claim language (i.e., as it relates to claims 1, 5-7 & 18-19).

One of ordinary skill in the art would not be enabled to use the invention as claimed for the following reasons: First, methods used to isolate the DRG11 gene, and an extrapolation to a "putative" function based solely on sequence homology, do not provide any indication that the gene encodes a protein with a particular function, nor does it clearly identify any such function. Second, the specification gives no indication that any change(s) occur in the pattern of expression of this gene or its encoded protein, or in the protein's function, in any working model that can be used to accurately define such function. Therefore, one skilled in the art would be unable to predict what effect(s) inducing or reducing expression of this gene or its encoded protein, or what effect(s) stimulating or blocking the action of the encoded protein would have on any cell or any organism. Third, there would be no reasonable expectation of success in using the claimed nucleic acid molecule, or vectors, or host cells in a method to solely produce this protein, because the specification provides no functional characterization of the DRG11 protein, nor any guidance or assays by which the skilled artisan could assess how to successfully use of this DRG11 protein. Moreover, it would require undue experimentation to develop such functional assays, or to perform subsequent analyses for determining how to use the discloses nucleic acid for encoding the DRG11 protein. It is noted that the sole written description for using the nucleic acid of SEQ ID NO 1 is to "provide a marker to identify neurons in the peripheral sensory lineage" (see page 2 of the specification). For these reasons, the specification is not enabled with respect to *how to use* the full scope of the claimed invention, because it would require undue experimentation to determine DRG11's function, and to then develop assays to distinguish those different proteins

from the instant invention that share homology with the DRG11 sequence, yet possess none of the intrinsic activities of a DRG11 protein; if and when such function is discovered.

The name "DRG11 protein " is defined on pages 5 and 9 of the specification as those proteins with an overall amino acid sequence homology that is "preferably greater than about 70%...", or "other proteins of the DRG11 family". The general recitation of the name "DRG11" or "nucleic acids which will hybridize to SEQ ID NO 1" (e.g., see pages 7-8 of the specification; as it relates to claim 3) is held, therefore, to encompasses any putative mutation, truncation/ fragment, substitution, addition, or deletion within any nucleic acid encoding a DRG11-related protein, or biologically functional equivalent of a DRG11 protein. However, the inclusion of any mutation within a nucleic acid that encodes DRG11 proteins sets forth no structural characteristics and little functional characterization. Moreover, the specification does not teach what amino acids are critical to maintaining a functional "DRG11 protein", or polynucleotides that encode such. Because the claims encompass deletions, insertions, and substitutions (conservative or non-conservative) and truncations/fragments of different nucleic acids that encode different DRG11 protein molecules, and because the specification fails to disclose what residues can be altered and still maintain the desired functional activity of the instant invention, the resultant random mutations to a nucleic acid encoding this protein would be predicted by the skilled artisan to result in inactive proteins. For example, Rudinger teaches that "it is impossible to attach a unique significance to any residue in a sequence. A given amino acid will not by any means have the same significance in different peptide sequences, or even in different positions of

the same sequence"(see page 3). Rudinger further states on page 6 that "the significance of particular amino acid sequences for different aspects of biological activity cannot be predicted *a priori* but must be determined from case to case by painstaking experimental study". Therefore, the lack of guidance provided in the specification, as to what alterations can be tolerated to maintain a functional DRG11 protein would prevent the skilled artisan from determining whether any DRG11 functionally equivalent molecule or hybridizable product could be made that retains the desired function of the instant invention, without undue experimentation to determine otherwise.

Overall, the issue is that no guidance is provided in the specification on what changes are tolerable to DRG11 to have a functional invention, or what functional properties DRG11 proteins possess. Nor can one extrapolate as to how to develop an assay to determine what, or if any function is associated with DRG11. Currently, the specification appears to merely constitute an invitation to experiment with isolated DRG11 nucleic acid products to discover DRG11's function. Therefore, it would not be expected that one of ordinary skill in the art would be able to successfully know *how to use* Applicants' invention, as claimed, based on the lack of guidance provided by the instant specification on DRG11's function, without undue experimentation to discover how to make and use Applicants' invention for these claimed embodiments related to producing DRG11-related proteins.

4. Claim 2 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Both SEQ ID NO. 1 and Figure 2 are nucleotide sequences, versus amino acid sequences as claimed. It is also suggested that because SEQ ID NO 1 is the same sequence as Figure 2, the redundant recitation of "Figure 2" should be deleted. In addition, it is suggested that amending the claims to "An isolated recombinant nucleic acid" would more accurately define the invention.

Claim Rejections - 35 U.S.C. § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-6 & 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Saito et al.

Saito et al. disclose a polynucleotide sequence that is 100% identical to SEQ ID NO 1 (i.e., Genbank Accession No. U29174, submitted June 14 1995; see pg. 291, 2nd *pp*; as it relates to claims 1 & 4). The amino acid sequence this nucleic acid molecule encodes is disclosed in Figure 3 (pg. 283; as it relates to claim 2). In that the DRG11 cDNA clones (pg. 282, last *pp*) were cloned into the *E.coli* λ ZapII expression vector, and screened (i.e., *E.coli* host cells transformed with the DRG11 clones), the limitations of claims 5-6 and 18 are anticipated by

Saito. In that the complimentary DNA sequence of these clones would inherently hybridize to SEQ ID NO 1, the limitations of claim 3 are also met. Finally, it should be noted that Saito et al. is four authors, versus the two inventors of the instant invention.

According to information provided by GenBank user services, sequences submitted to GenBank are processed and immediately placed into the public database unless the author(s) have requested that the sequences be withheld pending publication of an article. Processing typically takes from 2-3 days to a period of weeks. Sequences submitted to EMBL or DDBJ are transmitted to GenBank within 24 hours of their receipt. It therefore reasonably appears, absent evidence to the contrary, that the cited GenBank record was available to the public shortly after its submission date and constitutes prior art under 35 U.S.C. § 102 (b).

It is noted that this rejection is based in part upon a disclosure provided in a computer database record. Because the database was indexed so as to be available to the relevant part of the public, it is considered to be a U.S.C. § 102; see *In re Wyer*, 210 USPQ 790.

6. Claims 1 & 3 are rejected under 35 U.S.C. 102(b) as being anticipated by Liu et al.

Liu et al. disclose a recombinant nucleic acid that contains only 2 mismatches out of 40 nucleotides when compared to SEQ ID NO 1 (i.e., positions 577-616 in Fig. 1A, pg. 378), which would readily hybridize to the nucleic acid depicted in SEQ ID NO 1; thereby anticipating claim 3, as recited. In that the specification defines DGR11 proteins on page 6 to include sequences "shorter or longer than the amino acid sequences shown in the Figures", "portions and fragments

of the sequences shown in Figure 3", as well as "encoded by nucleic acids that will hybridize to the sequence depicted in Figure 2", Liu's nucleic acid molecule fullfills the criteria of a DRG11 equivalent, absent evidence to the contrary, as broadly claimed (i.e., as it relates to claim 1).

7. Claims 1 & 3 are rejected under 35 U.S.C. 102(b) as being anticipated by Cserjesi et al.

Cserjesi et al. disclose a recombinant nucleic acid that contains only 4 mismatches out of 51 nucleotides when compared to SEQ ID NO 1 (i.e., positions 574-624 in Fig. 3, pg. 1093), which would readily hybridize to the nucleic acid depicted in SEQ ID NO 1; thereby anticipating claim 3, as recited. In that the specification defines DGR11 proteins on page 6 to include sequences "shorter or longer than the amino acid sequences shown in the Figures", "portions and fragments of the sequences shown in Figure 3", as well as "encoded by nucleic acids that will hybridize to the sequence depicted in Figure 2", Liu's nucleic acid molecule fullfills the criteria of a DRG11 equivalent, absent evidence to the contrary, as broadly claimed (i.e., as it relates to claim 1).

Conclusion

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Robert Hayes whose telephone number is (703) 305-3132. The examiner can normally be reached on Monday through Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Paula Hutzell, can be reached on (703) 308-4310. The fax phone number for this Group is (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Robert C. Hayes, Ph.D.
November 18, 1997

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PRIMARY EXAMINER
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